# Decision Memo for Cryosurgery Ablation for Prostate Cancer (CAG-00031N)

## **Decision Summary**

(1) Approve coverage as primary treatment for clinically localized prostate cancer. (Stages T1-T3)

(2) Continue noncoverage for salvage therapy for local failures after radical prostatectomy, external beam irradiation, and brachytherapy

The Cover Issues Manual 35-96 will be modified to reflect this change in policy.

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### **Decision Memo**

TO: File: Cryosurgery Ablation of the Prostate

CAG Control No. 1998-00031N

FROM:

Grant P. Bagley, MD, JD Director, Coverage and Analysis

John J. Whyte, MD, MPH Medical Officer, Coverage and Analysis

RE: National Coverage Decision

DATE: February 1, 1999

This memo serves three purposes: (1) reviews the history of coverage policies for cryosurgery ablation of the prostate as a treatment for prostate cancer (2) analyzes recent developments including new scientific data; (3) delineates the reasoning in issuing a national coverage decision for localized prostate cancer. The decision in this memo is based upon a thorough review of all available scientific literature (both published and unpublished), lengthy discussions with the two manufacturers (Cryomedical Sciences and Endocare), numerous meetings and phone calls with Covance and members of the American Urological Association as well as the Society of Urological Cryosurgeons, discussions with various carrier medical directors and the urology work group, consultation with medical experts in urology including those who perform the procedure as well as those who do not, and various patients who have undergone the procedure and written to the agency

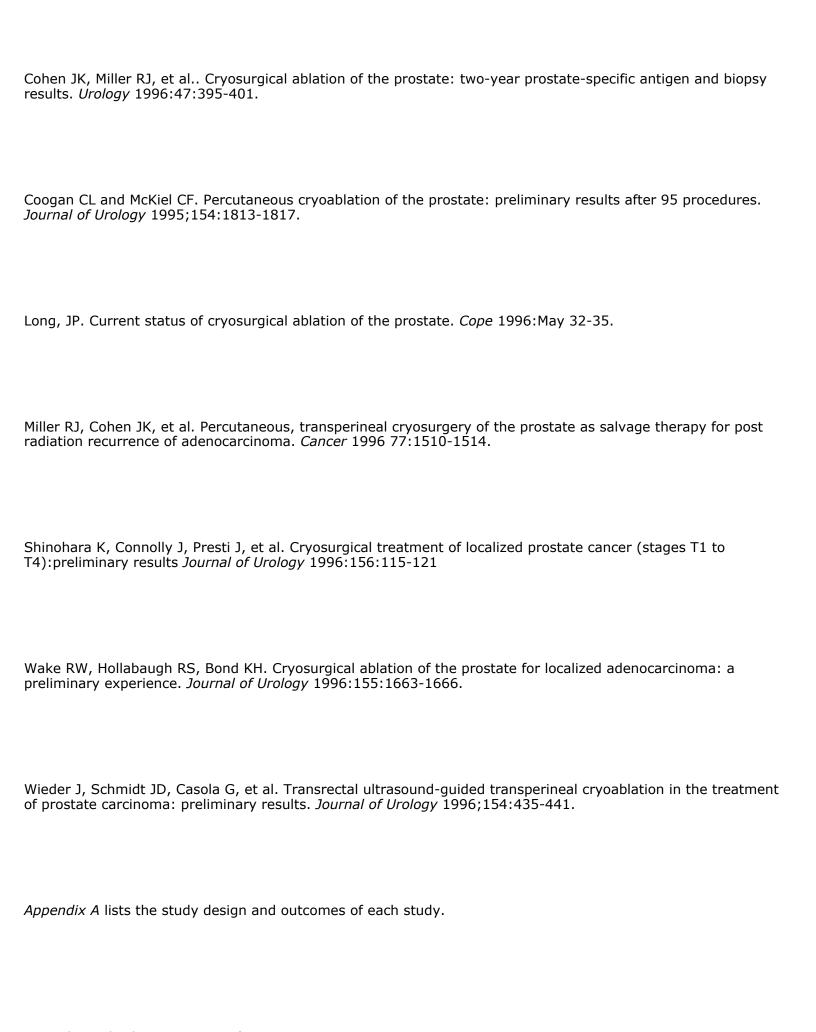
### **Background**

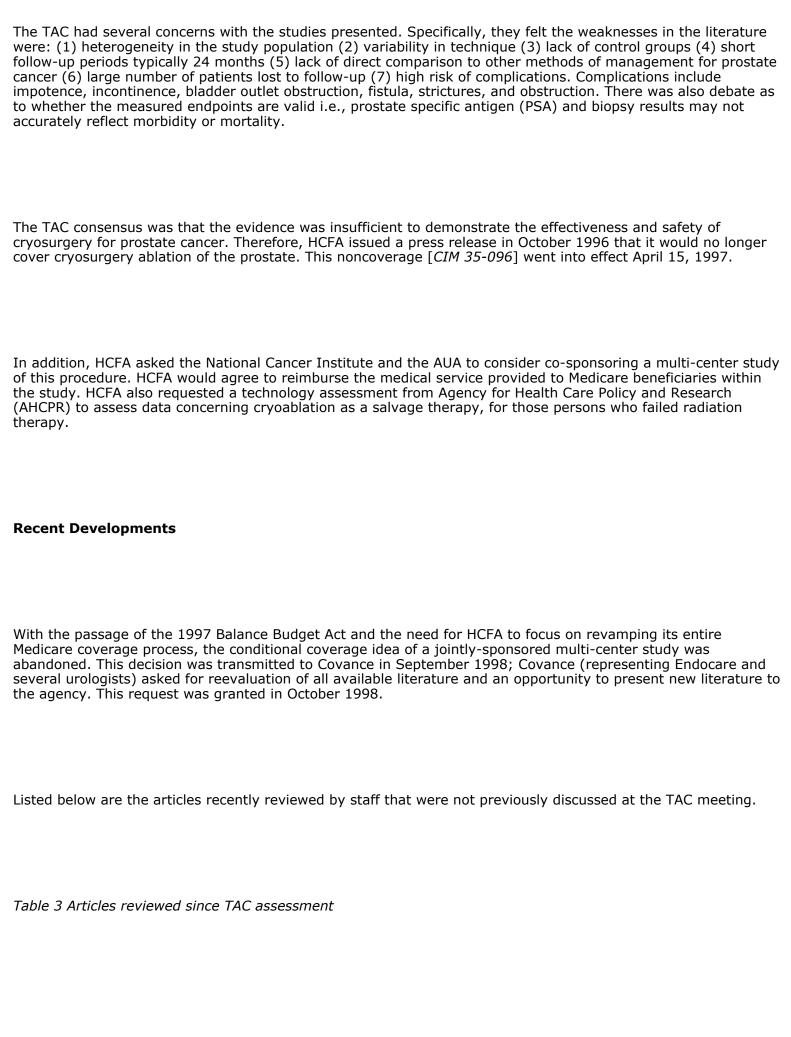
Prostate cancer is the most common cancer seen in men and is the second most common cause of cancer deaths in men, trailing lung cancer. According to the American Cancer Society, adenocarcinoma of the prostate accounts for 47% of all new cancers detected in men, with an incidence of 330,000 cases per year. The number of cases is expected to increase dramatically over the next decade as a result of the aging of the population as well as improvements in, and access to, methods of diagnosis. Despite the high prevalence of this disease, the management of localized cancer remains controversial, with no standard clinical treatment algorithm. The two most common therapies are surgery (i.e., radical prostatectomy) and external beam radiotherapy. Within the past few years, brachytherapy and cryosurgery have gained attention as an alternative to surgery or radiation. Hormonal therapy is usually reserved for the symptomatic patient with systemic disease. Treatment and prognosis vary dependent upon the stage of cancer.

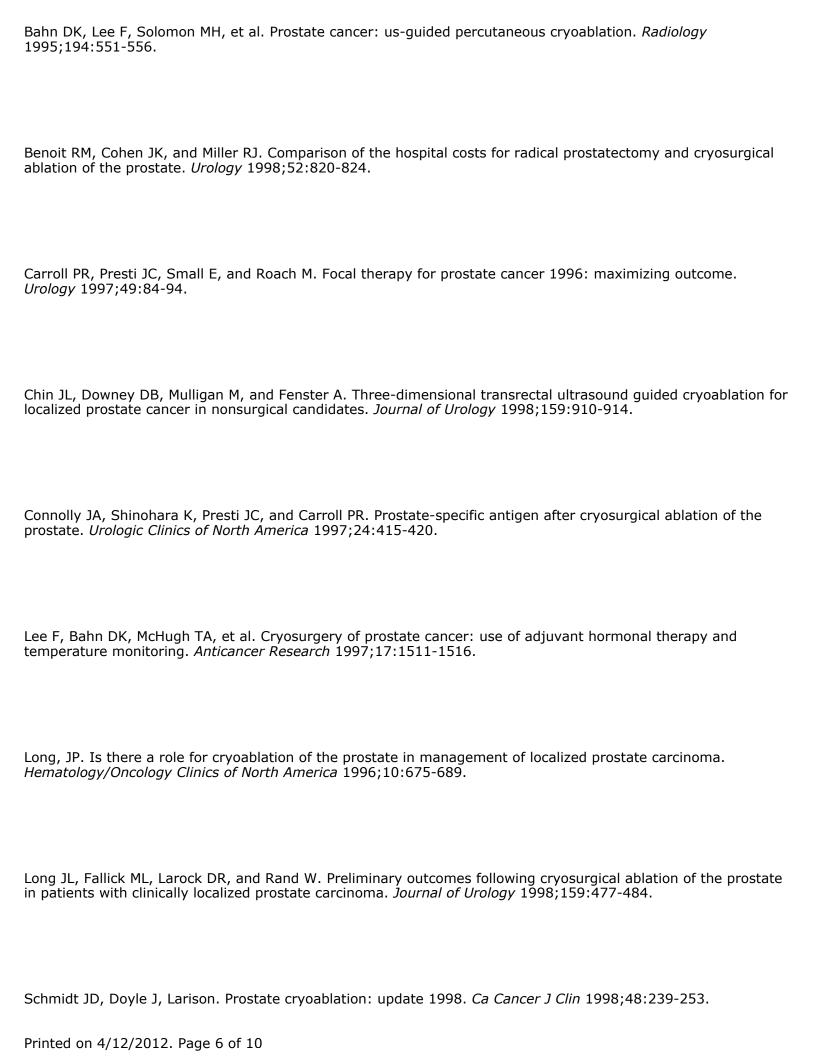
Table 1: Staging

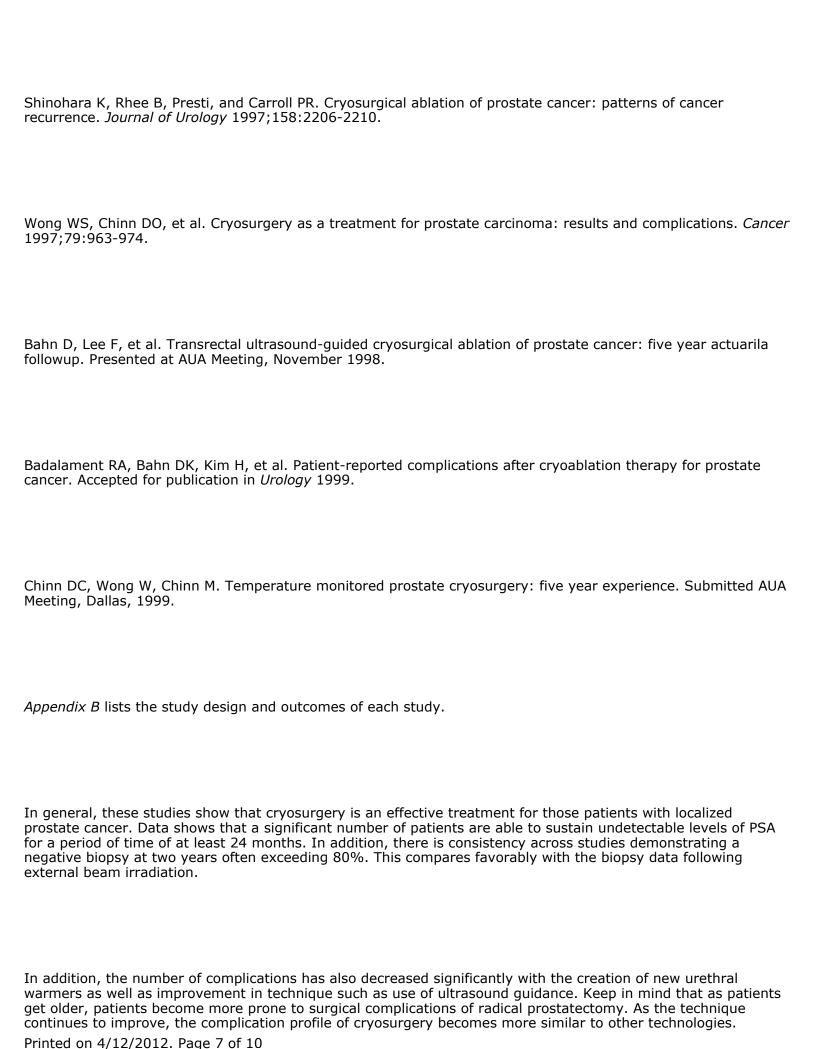
Pathology	TNM
Digitally unrecognizable cancer <5% of turp specimen, low to medium grade >5% of TURP specimen, or high-grade tumor Tumor detected by elevated PSA Digitally palpable cancer, organ confined <½ of one lobe >½ of one lobe	T1 T1A T1B T1C T2 T2A T2B
Cancer extending beyond prostate capsule Metastases	T3 N or M
To lymph nodes	N1-N3
Distant	M1-2











It is important to acknowledge that the scientific literature related to treatment of prostate cancer has flaws. There are few randomized trials, few patients enrolled in studies, and differences in outcome measures. For instance, the radiation oncology literature typically uses PSA < 1.0 ng/mL as evidence of a disease-free state whereas cryosurgery usually uses < 0.4 mg/mL as evidence of absence of disease. If one were to use PSA < 1.0 ng/mL as the reference in cryosurgical studies, cryosurgery would be more effective in obtaining PSA values less than 1.0 ng/mL. In addition, the technique used in radiation therapy has evolved over the past few years; therefore, the five year rates quoted in other therapies do not accurately reflect the treatment technology that exists today. The data exhibited by cryosurgery at this point is as effective as other technologies demonstrated early-on.

Of note, several providers who were lukewarm on cryosurgery have now become supportive. For instance, Dr. Fred Lee who is a prominent radiologist performing cryosurgery stated in 1995 that data was not clear. Three years later, he now believes the data is compelling and has opined a letter to the agency stating such. In 1996, Dr. John Long, a urologist from Boston, wrote that this technique was investigational. By 1998, Dr. Long has become one of cryosurgery's strongest supporters and has presented data to the agency that is outlined later in this memo.

By early October 1998 AHCPR had finished its assessment of cryosurgery as salvage therapy for those patients who had previously undergone radiation. This assessment concluded that although "cryosurgery has resulted in the biochemical disease-free survival of some patients who have had recurrent prostate cancer following radiation therapy, the effectiveness in salvaging such patients remains unclear because the number of patients treated has been small and the follow-up periods have been relatively short".

On December 9, 1998, John P. Long, MD, Director of Urologic Oncology and Assistance Professor of Medicine, Tufts University, New England Medical Center, presented pooled data from several studies. In data soon to be published, Dr. Long showed that current 5-year biochemical free survival outcomes for cryosurgery exceed 70%, which is comparable to radiotherapy and brachytherapy. A study of 206 patients had a 5-year biochemical survival of 78% for stages T1-T2. In a pooled retrospective analysis of 988 patients treated with cryosurgery from 5 institutions from 1993-1998, 82% of biopsies were negative. In addition, in a review of 445 consecutive patients with localized prostate cancer who received cryosurgery as primary therapy, conducted by Balm and Lee in Michigan, five year actuarial biopsy-proven disease free rate was 79%. Biochemical disease-free rate at the PSA < 0.5 ng/mL threshold was 76% for T1-T2 and 56% for T3-T4. This compares favorably to other therapies. In a study by Chinn in California, he calculated actuarial disease-free rates for 83 patients with localized prostate cancer who underwent cryosurgery, demonstrating an 80% disease-free state.

### **DECISION:**

	2) Continue noncoverage for salvage therapy for local failures after radical prostatectomy, external beam rradiation, and brachytherapy								
-	The Cover Issues Manual 35-96 will be modified to reflect this change in policy.								
3	Cryosurgery is safe, effective, as well as medically necessary and appropriate in certain patient populations specifically, those patients with Stages T1-T3 prostate cancer. It has demonstrated effectiveness through an absolute analysis as well as through a comparative analysis. Its results are comparable to brachytherapy and external beam radiation.								
t	hose patients wi	ho aŕe ι	indergoing this	procedure a		specific coverage polic by for clinically local able I]			
(	The national noncoverage policy will remain intact for salvage therapy. Although such patients often have few options and may actually be the most likely to benefit from this technique, the data still does not clearly support its effectiveness and appropriateness. As more data becomes available, this decision will be reviewed.								
	Authors/Year	Type of Study	Outcomes Studied	Number of Patients	Patient Characteristic	Results	Clinical Applications		
	Long, JP, Fallick ML, et al. <i>Journal of Urology</i> 1998	Case Series	Serum PSA changes, random prostate biopsies	145 patients avg followup 36 months	Average age 65.6 years  clinical stages T1 -T3	Actuarial rate for PSA <0.3 at 42 months was 59%. Crude rate at 24 months was 73%. Of 160 biopsies, 84% no cancer. 85% no clinical morbidity	outcomes for		

Average age: 62

years

Chin JL, Downey DB, Mulligan M, and

Case

series

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Serum PSA

levels at 6

months

52

patients

(1) Approve coverage as primary treatment for clinically localized prostate cancer. (Stages T1-T3)

Authors/Year	Type of Study	Outcomes Studied	Number of Patients	Patient Characteristic	Results	Clinical Applications
Journal of Urology 1998 Canada		Prostate biopsy at 3, 6, 12, 24 months	Followup ranged from 1-30 months.	Stages T1-T3 45 failed radiotherapy 7 deemed nonsurgical candidates	At 6 months, 11 patients had PSA <0.2. Numerous patients lost to followup. Minimal statistical testing performed. Only 70% of scheduled biopsies were performed	3d transrectal ultrasound appears to be feasible and worthwhile. Results similar to other studies. However, limited followup.
Wong WS, Chinn DO, et al. <i>Cancer</i> 1997 California		PSA levels at 3, 6, 12, 18, 24, and 30 months  Biopsies at 3-6,12-18, and 24 months.	98% patients were	Average age 69 years  Clinical stages II-IV	Median PSA dropped by 95% to 0.3 ng/mL 30 months after surgery. At 24 months, 92% negative biopsy. Negative biopsies 90% for pts who had temp monitoring. Negative biopsy only 17% for patients who had no temp monitoring.	Importance of temp monitoring noted. Significant negative biopsy results as well as biochemical evidence of disease-free state.
Bahn DK, Lee F, Solomon MH <i>Radiology</i> 1995 Michigan	Case series	Biopsy at 3, 6, 12 months PSA levels at 3, 6, 12 months	210 patients	Average age: 67 years  Localized prostate CA [diff staging system used]  Mean PSA preop 12.6	Negative biopsy at 12 months 97%  Mean PSA decreased from 12.6 to 0.43 at 12 months	Number of patients in disease free state at 12 months is impressive.
Shinohara K, Rhee B, Presti, and	Case series	PSA levels at 3,6,12 months and	134 patients	Average age: not specified	undetectable PSA and negative biopsy	Determined what PSA levels indicate low risk of
Carroll PR. Journal of Urology 1997  California		every 6 months thereafter  Biopsy at 6 months or with evid of biochemical failure	Mean followup: 17.6 months (range 3- 36 months)	Preop PSA ranged from 0.9 to 158 [avg19] Staging T1-T4	at 36 months. 87% patients undetectable PSA and 98% negative biopsy rate at 12 months.	recurrence. Neoadjuvant androgen blockade helpful for T-T2. PSA nadir of 0.4 should be obtained post cryo. Failures more often at apex and seminal vesicles.

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